In response to the Office Action dated **October 25, 2002**, please amend the above-identified application as follows:

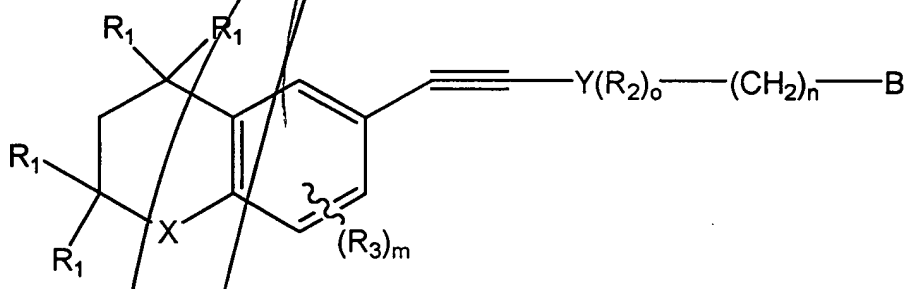
IN THE CLAIMS:

Cancel Claims 3, 4, 7, 8, 11, 12, 17, 18, 22, 23 28, and 29.

Amend Claims 1 and 14 as follows:

Claim 1 (twice amended)

A pharmaceutical composition for the treatment of a malignant disease or condition in a mammal, said condition being selected from the group consisting of breast cancer, colon cancer and leukemia, the composition comprising a pharmaceutically acceptable excipient and a therapeutically effective dose of a compound of the formula



where **X** is S or O;

R_1 is, independently, H or lower alkyl of 1 to 6 carbons;

R_2 and **R_3** are, independently, H, lower alkyl of 1 to 6 carbons, F, Cl, Br, I, alkoxy of 1 to 6 carbons, or fluoroalkoxy of 1 to 6 carbons;

m is an integer 0 to 3;

o is an integer 0 to 4;

n is 0-5;

Y is phenyl, naphthyl, or a heteroaryl group selected from a group consisting of pyridyl, thienyl, furyl, pyridazinyl, pyrimidinyl, pyrazinyl; oxazolyl, thiazolyl, or imidazolyl; and

B is COOH, a pharmaceutically acceptable salt thereof, CON$\mathbf{R_6R_7}$ or COO$\mathbf{R_8}$ where $\mathbf{R_6}$ and $\mathbf{R_7}$, independently, are hydrogen or an alkyl group of 1 to 6 carbons and $\mathbf{R_8}$ is alkyl of 1 to 6 carbons,

B1 said composition being adapted to be used in combination with another chemotherapeutic agent effective for the treatment of the malignant disease or condition of the mammal where the composition in combination with the other chemotherapeutic agent shows synergistic effect.

Claim 14 (twice amended)

A method of treating a malignant disease or condition in a mammal in need of such treatment, said condition being selected from the group consisting of breast cancer, colon cancer and leukemia, the method comprising the steps of:

administering to said mammal a pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective dose of a compound of the formula

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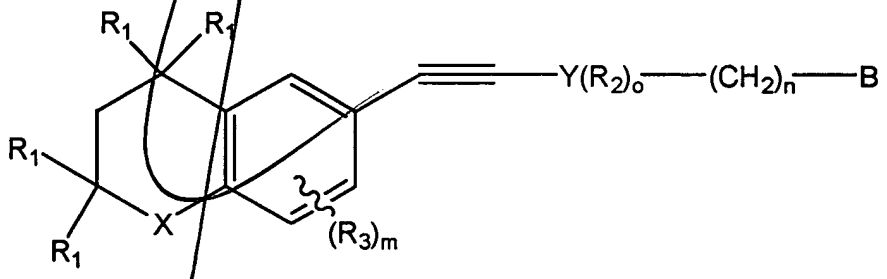

where **X** is S or O;

$\mathbf{R_1}$ is, independently, H or lower alkyl of 1 to 6 carbons;

$\mathbf{R_2}$ and $\mathbf{R_3}$ are, independently, H, lower alkyl of 1 to 6 carbons, F, Cl, Br, I, alkoxy of 1 to 6 carbons, or fluoroalkoxy of 1 to 6 carbons;

m is an integer 0 to 3;

o is an integer 0 to 4;

n is 0-5;

Y is phenyl, naphthyl, or a heteroaryl group selected from a group consisting of pyridyl, thienyl, furyl, pyridazinyl, pyrimidinyl, pyrazinyl; oxazolyl, thiazolyl, or imidazolyl;

B is COOH, a pharmaceutically acceptable salt thereof, CON$\mathbf{R_6R_7}$ or COO$\mathbf{R_8}$ where $\mathbf{R_6}$ and $\mathbf{R_7}$, independently, are hydrogen or an alkyl group of 1 to 6 carbons and $\mathbf{R_8}$ is alkyl of 1 to 6 carbons, and

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co-administering to said mammal with said compound another chemotherapeutic agent effective for the treatment of the malignant disease or condition of the mammal where the composition in combination with the other chemotherapeutic agent shows synergistic effect.

ADD THE FOLLOWING NEW CLAIMS 31 – 45

31. A pharmaceutical composition for the treatment of a malignant disease or condition in a mammal, said condition being selected from the group consisting of breast cancer and leukemia, the composition comprising a pharmaceutically acceptable excipient and a therapeutically effective dose of a compound of the formula

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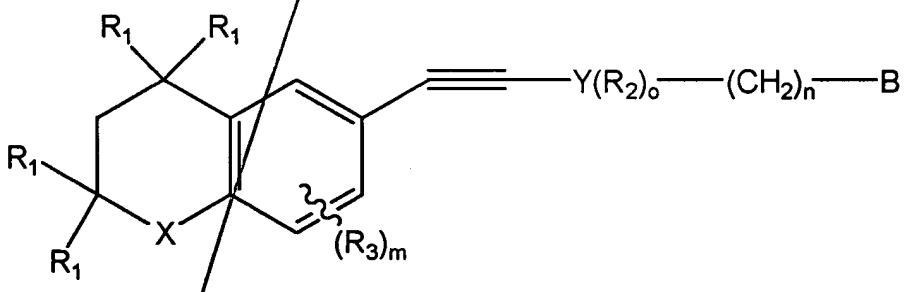


where **X** is S or O;

$\mathbf{R_1}$ is, independently, H or lower alkyl of 1 to 6 carbons;

$\mathbf{R_2}$ and $\mathbf{R_3}$ are, independently, H, lower alkyl of 1 to 6 carbons, F, Cl, Br, I, alkoxy of 1 to 6 carbons, or fluoroalkoxy of 1 to 6 carbons;

m is an integer 0 to 3;

o is an integer 0 to 4;

n is 0-5;

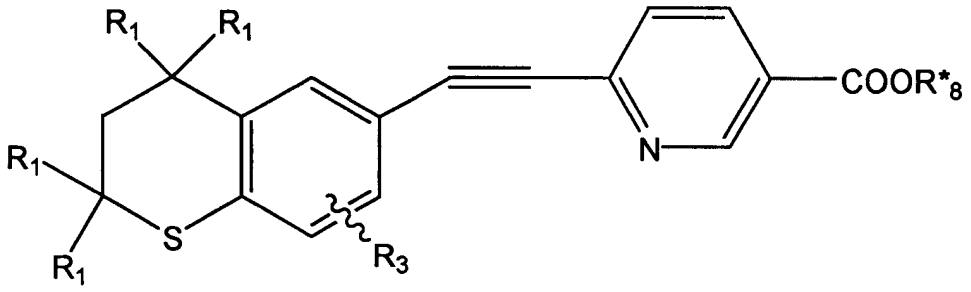
Y is phenyl, naphthyl, or a heteroaryl group selected from a group consisting of pyridyl, thienyl, furyl, pyridazinyl, pyrimidinyl, pyrazinyl; oxazolyl, thiazolyl, or imidazolyl; and

B is COOH, a pharmaceutically acceptable salt thereof, CON$\mathbf{R_6R_7}$ or COO$\mathbf{R_8}$ where $\mathbf{R_6}$ and $\mathbf{R_7}$, independently, are hydrogen or an alkyl group of 1 to 6 carbons and $\mathbf{R_8}$ is alkyl of 1 to 6 carbons,

said composition being adapted to be used in combination with another chemotherapeutic agent effective for the treatment of the malignant disease or condition of the mammal where the composition in combination with the other chemotherapeutic agent shows synergistic effect.

32. A pharmaceutical composition in accordance with Claim 31 where the other chemotherapeutic agent is interferon.

33. A pharmaceutical composition for the treatment of a malignant disease or condition in a mammal, said condition being selected from the group consisting of breast cancer and leukemia, the composition comprising a pharmaceutically acceptable excipient and a therapeutically effective dose of a compound of the formula

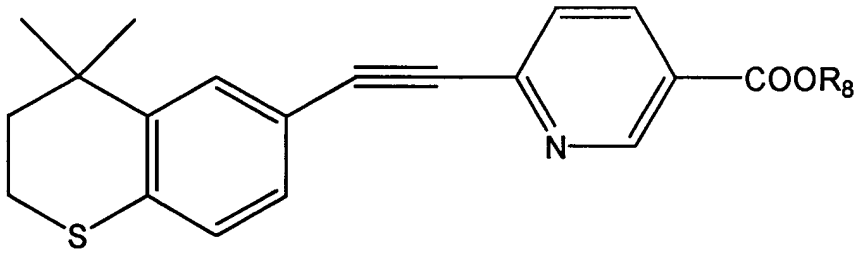


where $\mathbf{R_1}$ is H or methyl, $\mathbf{R_3}$ is H or methyl, and $\mathbf{R^*_8}$ is H, or lower alkyl of 1 to 3 carbons, or a pharmaceutically acceptable salt of said compound, said composition being adapted to be used in combination with another chemotherapeutic agent effective for the treatment of the malignant disease or condition of the mammal

where the composition in combination with the other chemotherapeutic agent shows synergistic effect.

34. A pharmaceutical composition in accordance with Claim 33 where the other chemotherapeutic agent is interferon.

35. A pharmaceutical composition for the treatment of a malignant disease or condition in a mammal, said condition being selected from the group consisting of breast cancer and leukemia, the composition comprising a pharmaceutically acceptable excipient and a therapeutically effective dose of a compound of the formula

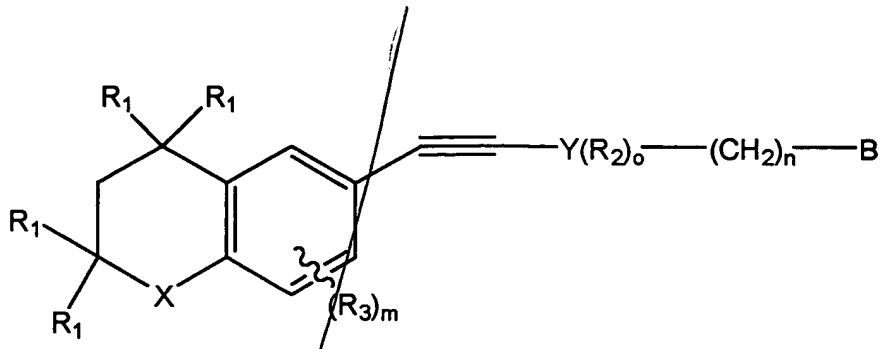


where R_8 is H, alkyl of 1 to 3 carbons, or a pharmaceutically acceptable salt of said compound, said composition being adapted to be used in combination with another chemotherapeutic agent effective for the treatment of the malignant disease or condition of the mammal where the composition in combination with the other chemotherapeutic agent shows synergistic effect.

36. A pharmaceutical composition in accordance with Claim 35 where the other chemotherapeutic agent is interferon.

37. A method of treating a malignant disease or condition in a mammal in need of such treatment, said condition being selected from the group consisting of breast cancer and leukemia, the method comprising the steps of:

administering to said mammal a pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective dose of a compound of the formula



where **X** is S or O;

$\mathbf{R_1}$ is, independently, H or lower alkyl of 1 to 6 carbons;

$\mathbf{R_2}$ and $\mathbf{R_3}$ are, independently, H, lower alkyl of 1 to 6 carbons, F, Cl, Br, I, alkoxy of 1 to 6 carbons, or fluoroalkoxy of 1 to 6 carbons;

m is an integer 0 to 3;

o is an integer 0 to 4;

n is 0-5;

B3 **Y** is phenyl, naphthyl, or a heteroaryl group selected from a group consisting of pyridyl, thienyl, furyl, pyridazinyl, pyrimidinyl, pyrazinyl; oxazolyl, thiazolyl, or imidazolyl;

B is COOH, a pharmaceutically acceptable salt thereof, $CONR_6R_7$ or $COOR_8$ where $\mathbf{R_6}$ and $\mathbf{R_7}$, independently, are hydrogen or an alkyl group of 1 to 6 carbons and $\mathbf{R_8}$ is alkyl of 1 to 6 carbons, and

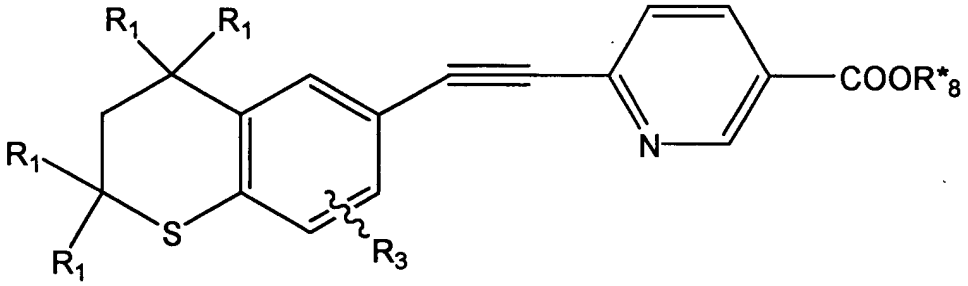
co-administering to said mammal with said compound another chemotherapeutic agent effective for the treatment of the malignant disease or condition of the mammal where the composition in combination with the other chemotherapeutic agent shows synergistic effect.

38. A method in accordance with Claim 37 where the chemotherapeutic agent is interferon.

39. A method in accordance with Claim 38 where the chemotherapeutic agent is human recombinant interferon α, human recombinant interferon β, or

human recombinant interferon γ.

40. A method of treating a malignant disease or condition in a mammal in need of such treatment, said condition being selected from the group consisting of breast cancer and leukemia, the method comprising the steps of:
administering to said mammal a pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective dose of a compound of the formula



where $\mathbf{R_1}$ is H or methyl, $\mathbf{R_3}$ is H or methyl, and $\mathbf{R^*_8}$ is H, or lower alkyl of 1 to 3 carbons, or a pharmaceutically acceptable salt of said compound, and

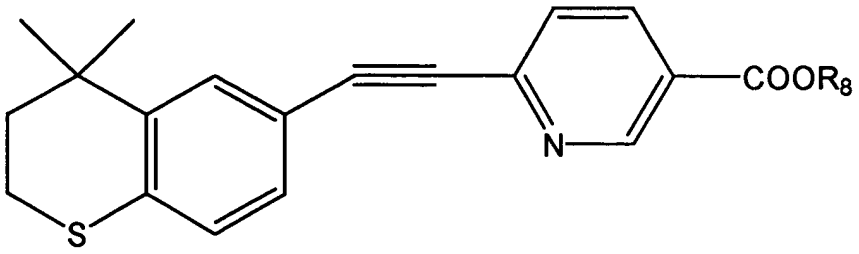
B3 co-administering to said mammal with said compound another chemotherapeutic agent effective for the treatment of the malignant disease or condition of the mammal where the composition in combination with the other chemotherapeutic agent shows synergistic effect.

41. A method in accordance with Claim 40 where the chemotherapeutic agent is interferon.

42. A method in accordance with Claim 41 where the chemotherapeutic agent is human recombinant interferon α, human recombinant interferon β, or human recombinant interferon γ.

43. A method of treating a malignant disease or condition in a mammal in need of such treatment, said condition being selected from the group consisting of breast cancer and leukemia, the method comprising the steps of:
administering to said mammal a pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective dose of a

compound of the formula



where R_8 is H, alkyl of 1 to 3 carbons, or a pharmaceutically acceptable salt of said compound, and

co-administering to said mammal with said compound another chemotherapeutic agent effective for the treatment of the malignant disease or condition of the mammal where the composition in combination with the other chemotherapeutic agent shows synergistic effect.

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44. A method in accordance with Claim 43 where the chemotherapeutic agent is interferon.

45. A method in accordance with Claim 44 where the chemotherapeutic agent is human recombinant interferon α, human recombinant interferon β, or human recombinant interferon γ.

REMARKS

The Rejection Pursuant To 35 U. S. C. Section 112, First Paragraph Has Been Obviated By The Present Amendment

Certain claims of the above-identified application were rejected because in the Examiner's opinion the data of the specification supported only treatment of breast cancer and leukemia with the compositions of the present invention in combination with another chemotherapeutic agent.

Applicant, acting through the undersigned attorney submits together with the present amendment a Declaration by one of the named inventor Allisar Nehme Ph. D. The Nehme Declaration together with the accompanying graphs establishes that the drug ethyl 6-[2-(4,4-dimethylthiochroman-6-yl)ethynyl]nicotinate (also known by its trade name TAZAROTENE®, referred to